Spatial distribution of end-stage renal disease (ESRD) and social inequalities in mixed urban and rural areas: a study in the Bretagne administrative region of France

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Original Article

Spatial distribution of end-stage renal disease (ESRD) and social inequalities in mixed urban and rural areas: a study in the Bretagne administrative region of France

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Abstract

Background. Several studies have investigated the implication of biological and environmental factors on geographic variations of end-stage renal disease (ESRD) incidence at large area scales, but none of them assessed the implication of neighbourhood characteristics (healthcare supply, socio-economic level and urbanization degree) on spatial repartition of ESRD. We evaluated the spatial implications of adjustment for neighbourhood characteristics on the spatial distribution of ESRD incidence at the smallest geographic unit in France.

Methods. All adult patients living in Bretagne and beginning renal replacement therapy during the 2004–09 period were included. Their residential address was geocoded at the census block level. Each census block was characterized by socio-economic deprivation index, healthcare supply and rural/urban typology. Using a spatial scan statistic, we examined whether there were significant clusters of high risk of ESRD incidence.

Results. The ESRD incidence was non-randomly spatially distributed, with a cluster of high risk in the western Bretagne region (relative risk, RR = 1.28, P-value = 0.0003). Adjustment for sex, age and neighbourhood characteristics induced cluster shifts. After these adjustments, a significant cluster (P = 0.013) persisted.

Conclusions. Our spatial analysis of ESRD incidence at a fine scale, across a mixed rural/urban area, indicated that, beyond age and sex, neighbourhood characteristics explained a great part of spatial distribution of ESRD incidence. However, to better understand spatial variation of ESRD incidence, it would be necessary to research and adjust for other determinants of ESRD.

Keywords: ESRD incidence; fine geographic scale; neighbourhood deprivation; spatial analysis

Introduction

Geographical variations of end-stage renal disease (ESRD) incidence have been established in the USA [1], Australia [2], Japan [3], UK [4], Denmark [5] and France [6]. The reasons for these variations have not been fully elucidated.

In the developed countries, leading causes of ESRD are related to demographic characteristics such as age, sex and comorbidities such as diabetes and hypertension. Several studies established the implication of these factors to the geographical variations of ESRD incidence [1, 7–10].

Some hypotheses suggested that several factors in the social environment may impact ESRD incidence, including rural/urban typology and neighbourhood deprivation [1, 6, 11]. Some researchers reported higher ESRD rates in rural compared with urban counties [1], whereas others studies suggested a higher ESRD rate in an urban area [6, 11]. Moreover, socio-epidemiological research documented a social gradient of ESRD [5, 11, 12]. Within developed countries, people from socio-economically disadvantaged areas were more likely to reach ESRD, compared with those from advantaged areas, who might benefit from chronic kidney disease (CKD) treatment before ESRD stage [2]. A few studies have reported that socio-economic factors explained geographic variation of ESRD incidence [4, 6, 13].

Nevertheless, despite insurance coverage, the poor access to healthcare resources has been reported to be a potential risk factor of ESRD [1, 4, 14, 15].

Although several studies have investigated the implication of biological and environmental factors on geographic variations of ESRD, at national [14, 16], regional [3, 5, 17],

counties [1], district [6] or census ward level [4], none of them assessed spatial implication of neighbourhood characteristics on spatial repartition of ESRD incidence.

In this study, we assessed the spatial pattern of ESRD incidence in the Bretagne administrative region of France at the smallest geographic unit (census block): we evaluated the spatial implications of adjustment for neighbourhood characteristics beyond age and sex (healthcare supply, deprivation and rural/urban typology) on the spatial distribution of ESRD incidence, using an appropriate spatial approach: the spatial scan statistic [18].

Materials and methods

Study design

The study was conducted in the Bretagne administrative region: an area located in western France, with 3 094 000 inhabitants in 2006. Analyses were conducted at the French census block level (called IRIS by INSEE, the French National Statistics Institute). A Bretagne region was subdivided into 1797 census blocks/IRIS, each having 2000 inhabitants on average.

Study population

We included all adult patients (aged above 18 years) living in Bretagne and beginning renal replacement therapy (RRT) between 1 January 2004 and 31 December 2009. This cohort was extracted from the French national registry 'Réseau Epidémiologie et Information en Néphrologie (REIN)' [19].

Data collection

The database included the patient's date of birth, date of first RRT and sex. Residential addresses of patients were collected and matched to the corresponding census blocks using map databases.

Rural/urban typology

The residential census block of each patient was classified into rural/urban classes, using an approach inspired from the study by Van Eupene *et al.* [20], in three consecutive steps:

(i) Classification of each census block into one of the three rural/urban classes based on Organisation for Economic Co-operation and Development (OECD) typology [21], using population density criteria.
(ii) Classification of each census block into one of the three rural/urban classes based on land cover criteria typology [22], using natural and artificial area criteria.
(iii) Combination of the population density and land cover criteria for final rural/urban classification.

The combined dataset consisted of nine rural/urban classes resulting from a combination of the three-by-three classes. This matrix can be seen as the final mathematical summarization of the full range of territorial variables into a 2D matrix. For use in the study, for which nine classes were too complex, the typology was thematically aggregated into four rural/urban classes: urban close-space, peri-urban, peri-rural and deep rural [23] (Figure 1a).

Socio-economic deprivation index

Socio-economic and demographic data were obtained from the 2006 census, conducted by INSEE at the census block level. To characterize the neighbourhood deprivation level, we used a deprivation index. This measure combined material and social aspects of deprivation to measure the overall socio-economic status. It included variables related to education, income, occupation, unemployment and immigration to cover and capture the different dimensions of the deprivation. Successive principal component analyses were conducted to create the deprivation index based on Lalloué *et al.* ('SesIndexCreatoR' Package) [24]. This procedure has provided its validity to demonstrate socio-economic gradients in the incidence of myocardial infarction and asthma attacks [25, 26] and in the infant mortality rate [27–29].

The socio-economic determinants of a rural area may be different from those of an urban area: so the socio-economic deprivation index was calculated in each rural/urban class considered here (urban close-space, peri-urban, peri-rural and deep rural). The level of neighbourhood deprivation was categorized into three groups according to the tertiles of the deprivation index distribution: low, moderate and high deprivation (Figure 1b).

Healthcare supply data

Addresses of all dialysis and transplantation centres of Bretagne were collected and matched to the census block level. We assigned to each census blocks the number of dialysis and/or transplantation centres.

Analysis

Spatial methodology. The cluster of ESRD incidence was analysed by means of a spatial scan statistic implemented in the SaTScan software [30]. This cluster analysis allowed exploration of the presence of high ESRD incidence clusters ('most likely clusters') and their spatial approximate location [28, 31].

In this approach, the null hypothesis (H_0) tested is that the risk of ESRD incidence is the same throughout the study area; in other words, the expected ESRD incidence would be randomly distributed in space [32, 33]. The alternative hypothesis (H_1) is that there is an elevated risk of ESRD incidence within the cluster in comparison with census blocks outside the cluster. The number of ESRD incident cases in each census block is assumed to follow a Poisson distribution.

The procedure works as follows: a circle or window of variable radius (from 0 up to 50% of the population size [18]) is placed at every centroid of the census block and moves across the whole study area, to compare the ESRD incidence in the window with incidence expected under a random distribution. The identification of the most likely clusters is based on a likelihood ratio test [34], with an associated P-value obtained using Monte Carlo replications [33].

If we detect significant cluster using this method, a logical next step is to see whether the significant cluster can be explained by suspected risk factors. Thus, spatial analyses were performed in four stages (step by step):

(i) Unadjusted analysis, to identify and localize the most likely cluster of high incidence of ESRD.
(ii) Adjusted analysis for age and sex.

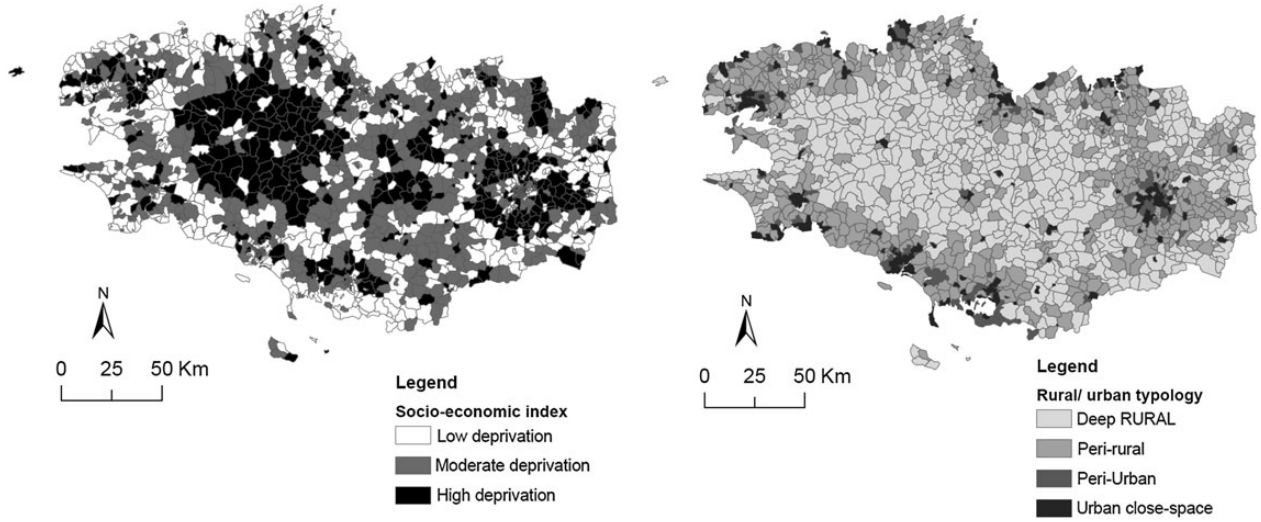

Fig. 1. Spatial distribution of urban/rural typology (**a**) and spatial distribution of the neighbourhood socio-economic deprivation index (**b**) across the Bretagne administrative region.

Table 1. Repartition of ESRD cases according to neighbourhood socio-economic deprivation

Neighbourhood socio-economic deprivation category	Patients beginning dialysis ($N = 2006$)			Pre-emptive transplanted patients ($N = 66$)			All patients ($N = 2072$)
	N (%)	Mean age	Sex ratio[a]	*N* (%)	Mean age	Sex ratio[a]	
Low deprivation census blocks ($n = 600$)	375/2006 (18.7%)	64.42	1.70	16/66 (24.2%)	45.25	3	391
Moderately deprived census blocks ($n = 598$)	628/2006 (31.3%)	67.42	1.57	25/66 (37.9%)	49.96	0.56	653
Highly deprived census blocks ($n = 599$)	1003/2006 (50%)	68.38	1.45	25/66 (37.9%)	47.64	1.5	1028

N: number of patients; *n*: number of census block in each categories.
[a]Men versus women.

(iii) Adjusted analysis for age, sex and rural/urban typology.
(iv) Adjusted analysis for age, sex and socio-economic deprivation index.
(v) Adjusted analysis for age, sex, socio-economic deprivation index and healthcare supply.

Results

We collected data on 2072 incident cases living in Bretagne and beginning RRT in the 2004–09 period, including 2006 patients starting dialysis and 66 cases of pre-emptive transplantation. The crude annual ESRD incidence rate in the Bretagne administrative region was equal to 142 per million inhabitants (>18 years).

Table 1 summarizes that, among pre-emptive transplanted patients, 38% were living in census blocks with moderate socio-economic deprivation and 24% in those with low deprivation, whereas 50% of patients beginning a dialysis were issued from most disadvantaged census blocks.

Briefly, Figure 2 details the census blocks containing the most likely clusters of high risk of ESRD incidence, their spatial location and spatial shift of centroid from unadjusted cluster to covariate-adjusted cluster. Table 2 presents the most likely clusters, the number of census blocks, radius and relative risk (RR, the ratio of the observed-to-expected number of new patients in each census blocks estimated by SaTScan) for each cluster.

(i) *Unadjusted analysis*, Figure 2a reveals the location of the most likely and the secondary clusters. The most likely cluster, in the western Bretagne region, had a risk of ESRD incidence 1.28 greater than the rest of Bretagne (P-value = 0.0003; Table 2). The small secondary cluster, identified in the immediate north-eastern part of Bretagne (Saint-Malo area), was also statistically significant (P-value = 0.039).
(ii) *After adjustment for age and sex* (Figure 2b), the most likely significant cluster was reduced in north-western Bretagne (RR = 1.29). The centroid of the cluster shifted and the likelihood ratio decreased from 15.94 to 10.96 (Table 2), which indicate that age and sex explained some of the excess risk of ESRD incidence observed in the unadjusted analysis. The secondary cluster, identified in crude analysis in the north-eastern part of Bretagne (Saint-Malo area), disappeared after adjustment for age and sex. These results may be explained by an important retired population living in this region.

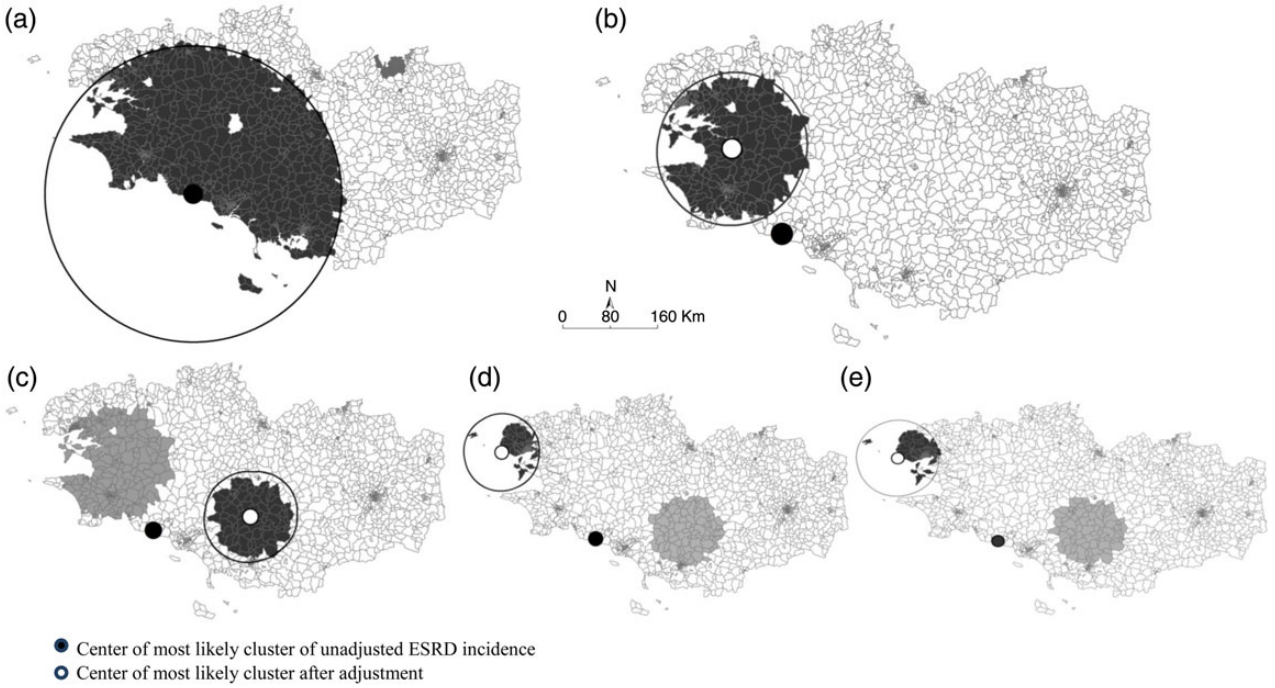

Fig. 2. Spatial relocation of the most likely cluster of unadjusted ESRD incidence (**a**); after adjustment for sex and age (**b**); age, sex and rural/urban typology (**c**); age, sex and deprivation index (**d**); age, sex, deprivation index and healthcare supply (**e**). (b–e) Different spatial variability of ESRD incidence compared with the results from the crude analysis (a) and spatial shift of the centroid of the cluster from western Bretagne region (a) to north-western Bretagne when adjusted for age and sex alone (b) to south-western Bretagne when adjusted for age and sex and rural/urban typology (c), to extremely western Bretagne when adjusted for age and sex, deprivation index and healthcare supply (d and e). Two clusters are revealed in (c, d and e): the grey one is the secondary non-significant cluster and the black one is the primary significant cluster.

Table 2. Summary statistics of the most likely clusters spatial relocation resulting from the adjusted analysis

Analysis	Confounders	Cluster radius (m)	No. of census blocks/no. of inhabitants in the cluster	No. of expected cases	No. of observed cases	RR	LLr	P-value
Unadjusted[a]								
	1. No adjustment	90638.08	731/1 314 321	884.97	1013	1.28	15.94	<0.001
Adjusted[b]								
	2. Sex, age	38961.10	282/542 172	362.68	446	1.29	10.96	0.02
	3. Rural/urban typology, sex, age	27176.50	88/151 809	98.22	150	1.50	12.41	0.006
	4. SES[c] level, sex, age	28474.75	121/261 220	156.06	218	1.44	11.93	0.009
	5. Healthcare supply, SES[c] level, sex, age	29250.53	125/269 374	162.76	224	1.42	11.28	0.013

RR: relative risk; LLr: log likelihood ratio.
[a]Unadjusted analysis, to identify and localize the most likely cluster(s) of high risk of ESRD incidence.
[b]Adjusted analysis for (2) sex and age; (3) sex, age and rural/urban typology; (4) sex, age and socio-economic deprivation index; (5) sex, age, socio-economic deprivation index and healthcare supply.
[c]Socio-economic deprivation index.

(iii) *After adjustment for age, sex and rural/urban typology* (Figure 2c), the most likely significant cluster shifted in South-western Bretagne (RR = 1.5), a deep rural zone. The likelihood ratio decreased from 15.94 to 12.41 (Table 2). These results indicated that age, sex and rural/urban typology explained a great part of the excess risk of ESRD incidence observed in the unadjusted analysis.

(iv) *After adjustment for age, sex and deprivation index* (Figure 2d), the most likely significant cluster shifted in a small location in extremely western Bretagne (RR = 1.44), close to Brest city. The likelihood ratio decreased from 15.94 to 11.93 (Table 2).

(v) *After adjustment for age, sex, deprivation index and healthcare supply* (Figure 2e), the most likely cluster was always significant and located in the same zone in extremely western Bretagne (RR = 1.42). However, the likelihood ratio decreased from 15.94 to 11.28 (Table 2).

These results indicated that the excess risk of ESRD incidence observed in the unadjusted analysis was explained in a great part, but not entirely, by age, sex, healthcare supply and socio-economic deprivation taking into account rural/urban typology.

To explain the location of the most likely cluster, the presence of diabetes and cardiovascular diseases and estimated glomerular filtration rate (eGFR) at dialysis start (mL/min) were compared between patients living in the cluster of high incidence and other patients. Except for

eGFR at dialysis start, no other significant difference was found between these two groups (diabetes rate 29 versus 25% and cardiovascular diseases 59 versus 54% within and outside of the cluster, respectively). The median eGFR of patients living in the cluster was 9.2 mL/min at dialysis start, whereas it was 8.1 mL/min for the other patients ($P < 0.0001$).

Discussion

To our knowledge, such a work, exploring spatial implication of neighbourhood characteristics on geographical variations of ESRD incidence at such small-scale level had never been performed. That's why it is difficult to compare our findings with those of others.

Our study revealed that ESRD incidence was not randomly distributed in Bretagne. The increased ESRD incidence on western Bretagne was statistically significant, but age, sex and social deprivation index had to be taken into account in the interpretation of ESRD incidence. Otherwise, while some RRs were similar when adjusting for different covariates, the position of cluster could vary greatly. The RR of ESRD incidence cluster, adjusted for sex and age and rural typology (Figure 2c) was 1.5, whereas the RR of age/sex and deprivation-adjusted cluster (Figure 2d) was 1.44. However, the two clusters were located at significantly different distances from original cluster (Figure 2a) and contained different numbers of census blocks. This finding indicated a spatial shift in risk after adjustment for risk factors [31].

Not surprisingly, age and sex explained a great part of the spatial variations of ESRD incidence across different census blocks. Several studies showed that age and sex were important risk factors for ESRD. In USA, the annual incidence of ESRD was twice as high in males as females up to 75 years [35] and the RR of ESRD increased with age more sharply in males than females [11]. It is well known that renal function declines with age [36]. Older people are particularly susceptible to kidney damage due to age-related decline in glomerular filtration or due to chronic disease such as, diabetes, hypertension, glomerular and tubulo-interstitial disorders [37, 38].

Moreover, interestingly, the neighbourhood deprivation index taking into account the rural/urban typology explained a great part of spatial repartition of the excess risk of ESRD incidence observed in the crude analysis.

These findings are coherent with previous works [4, 6] and consistent with a number of earlier research documenting a social gradient of renal disease such as ESRD, RRT [4, 5, 12] or CKD [39]. Some of these reports showed an inverse association between ESRD incidence or RRT and various deprivation measures such as income [5, 6, 11, 40], education [5], composite socio-economic score [4, 12, 13], poverty [41] and unemployment [6]. However, these findings were controversial since not confirmed by other studies [6, 42]. Most studies suggested that socio-economic status was a potential determinant of access to healthcare [8]. However, in France, the access to diagnosis and treatment of ESRD should not be limited by socio-economic status. Medical and hospital costs for patients with ESRD are completely covered (100%), and the reimbursement is regulated by uniform rates regardless of whether the patient is treated in the public or private nephrology facility.

Nevertheless, beyond access to healthcare, some studies hypothesized that socio-economic status could be a potential determinant of factors that might influence the occurrence and progression of CKD such as:

(i) a better preventive medical care: in our study, 25 of the 1028 patients (2%) living in the most disadvantaged census blocks were pre-emptively transplanted, while this number increased to 4% (16/391) for those living in the most advantaged census blocks (Table 1). These advantaged patients might have access to better prevention and early referral to a nephrologist facilitating access to pre-emptive renal transplantation;
(ii) lack of availability of healthy nutrition, exposure to environmental nephrotoxins [13, 43] in deprived neighbourhood;
(iii) prevalence and management of pathologies leading to ESRD like hypertension [44–46] and diabetes [47].

Finally, our findings showed that it remained a significant cluster of excess risk of ESRD incidence, not explained by sex, age, neighbourhood deprivation, rural/urban typology and healthcare supply. This difference cannot be explained by Bretagne residents followed by facilities exterior of Bretagne, because our region is limited by sea from three sides and almost all ESRD patients living in Bretagne are followed by the nephrology facilities in the region.

Our finding suggests that the observed cluster of elevated ESRD incidence may be in part due to differences in clinical practice patterns of nephrologists on the dialysis start timing. As lower eGFR is associated with higher mortality, the risk of mortality before RRT initiation could be higher among ESRD patients living out of the cluster. This fact could explain partially the higher incidence of RRT initiation in the cluster of interest. The cluster of elevated ESRD incidence may also be due to population health status.

To explain the cluster of excess risk, it would be necessary to carry out studies with other characteristics of Bretagne's inhabitants: prevalence of hypertension [10, 48], diabetes [7, 8, 49], cardiovascular disease [9] and accessibility to healthcare [1, 4, 14, 15]).

Strengths and limitations

One strength of this work is the use of small area-level analyses allowing a correct understanding of the geographic patterns of ESRD incidence. Moreover, this type of analysis is essential for revealing local-level inequalities that are often masked when analysis is produced at large area scales.

Another strength of our study is the use of an appropriate spatial approach that allowed us to (i) identify areas of significantly elevated risk of ESRD incidence and (ii) investigate spatial implications of adjustment for neighbourhood characteristics. This approach constitutes a useful screening tool to detect clusters of high risk of ESRD for further investigations.

Furthermore, we developed a neighbourhood deprivation index according to urban/rural typology, which was more appropriate than classic indices such as Carstairs and Townsend typically used to investigate health inequality in the urban area. These indicators show some weaker associations with the health indicators observed in rural areas.

One limitation of our work is the absence of other population characteristics like health status. Another

limitation is the lack of individual socio-economic status. However, we chose a fine geographical scale, designed to be as homogeneous as possible in terms of population size and socio-economic characteristics. The homogeneity of the census block ensures minimization of ecological bias. The results issued from this spatial-level analysis are considered to be close to what can be observed at the individual level [50]. Finally, this study concerned the patients beginning an RRT, so ESRD patients who were not referred to nephrologist or refused RRT were not included in our analysis.

Conclusions

We conducted a spatial analysis of ESRD incidence at a fine scale across a mixed rural/urban area with adjustment for deprivation determinants of ESRD. Our results indicated that, beyond age and sex, neighbourhood characteristics explained a great part of spatial distribution of ESRD incidence. However, to better understand spatial variation of ESRD incidence, it would be necessary to research and adjust for other determinants of ESRD.

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Conflict of interest statement. None declared.

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